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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/417,478	10/13/1999	JOHN MCCAFFERTY	05569.0004.DVUS07	8812

22930 7590 04/01/2009

HOWREY LLP - East
C/O IP DOCKETING DEPARTMENT
2941 FAIRVIEW PARK DR, SUITE 200
FALLS CHURCH, VA 22042-2924

EXAMINER	
LIU, SUE XU	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
04/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/417,478	MCCAFFERTY ET AL.	
	Examiner	Art Unit	
	SUE LIU	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45,46 and 48-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45,46 and 48-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/16/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Claims 1-44 and 47 have been canceled.

Claims 45, 46 and 48-54 are currently pending.

Claims 45, 46 and 48-54 are being examined in this application.

Priority

2. This application appears to be a Divisional of U.S. Patent Application Nos. 08/484,893 (filed 6/07/1995), which is now a US PATENT, 6,172,197, which is a CON of 07/971,857 (filed 1/8/1993; now US PAT 5,969,108), which is a 371 of PCT/GB91/01134 (filed on 7/10/1991).

Claim Rejection(s)/Objection(s) Maintained

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(Note: the instant claim numbers are in bold font.)

Ladner ('409)

4. Claims 45, 46 and 48-54 are rejected under **35 U.S.C. 102(e)** as being anticipated by Ladner et al (US 5,223,409; filed 3/1/1991; priority date: 9/2/1988; cited in IDS filed 2/1/2001).

The instant claims recite the followings:

Recombinant host cells each of which harbors a phagemid comprising a nucleic acid Fragment encoding one member of a specific binding pair fused to a nucleic acid encoding a gene III coat protein surface component of a filamentous bacteriophage and further comprising an origin of replication of a filamentous bacteriophage, the gene III coat protein surface component encoding nucleic acid and the origin of replication being the only nucleic acid in the phagemid derived from filamentous bacteriophage, whereby the host cells collectively harbor in the phagemids a library of nucleic acid fragments encoding a genetically diverse population of the specific binding pair members, each member of the specific binding pair capable of being expressed as e. fusion protein with the gene III coat protein surface component of a filamentous bacteriophage so that each member of the specific binding pair comprises a functional specific binding domain for its complementary specific binding pair member and whereby *upon infection of said recombinant host cells with a helper phage, the phagemids are each packaged into filamentous bacteriophage particles displaying on their surface the functional specific binding pair member as a fusion with the gene III surface component of the filamentous bacteriophage and whereby each filamentous bacteriophage has a coat partially derived from the helper phage and partly from said fusion.*

The instant claims are drawn to recombinant cells comprising phagemid comprising: 1.) phage origin of replication; 2.) gene III coat protein surface component; 3.) gene encoding for "a

specific binding pair" fused to gene III. The portion of the instant claim 54 in italic (shown above) is a recitation of intended use, which does not result in additional structural limitations to the instant claimed "recombinant cells".

Ladner et al, throughout the patent, teach using phage display to express binding domains (Abstract).

The reference teaches inserting a nucleic acid encoding for a binding domain (e.g. claim 1), which the antigen reads on the "one member of a specific binding pair" of **clm 54**.

The reference teaches using filamentous phage and fusing the antigen with the Gene III coat protein (e.g. cols. 5-6), which reads on the phage and the gene III coat protein of **clm 54**.

The reference also teaches using host cells to grow the phage particles (e.g. col. 6, lines 1+), which reads on the "recombinant host cells" of **clm 54**.

The reference also teaches methods of displaying binding proteins on the surface of filamentous bacteriophage via nucleic acid sequences including gIII and screening for target molecule binding wherein phagemids and helper phage may be utilized (please refer to entire document particularly abstract; columns 1, 4-12, 15-105; Examples I-XVI; claims 1-66). Ladner et al. teach phagemid vectors particularly phagemid vectors pBluescript® K/S and pGEM®-3Zf (see column 76; lines 55-67; column 77, lines 1-4; column 106), which inherently contains only ori from filamentous bacteriophage, as evidenced by the Promega Technical Bulletin (Promega Technical Bulletins for pGEM®-3Zf(-) and pGEM®-3Zf(+); Downloaded from Promega website on 1/11/08) and/or the Stratagene Instruction Manual (Stratagene Instruction Manual for pBluescript® II phagemid vectors; downloaded from Stratagene website on 1/11/08). The

construct comprising gIII-binding domain would be inserted into the multiple cloning site of the said vector (as taught by the reference) for phage display (i.e. plasmid would then contain only ori and gIII of filamentous bacteriophage; please refer to columns 53-59, section IV.B).

The reference also teaches mutating the insertions (e.g. cols. 31-32), which reads on the limitation of **clm 45**.

The reference also teaches displaying single chain antibodies using phage display (e.g. cols. 6-7), which reads on the immunoglobulin binding domains and the scFv of **clms 46**, and **48-53**.

Discussion and Answer to Argument

5. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants assert the Ladner reference does not teach a phagemid vector comprising gIII. (Reply. pp.5+)

Ladner et al. teach phagemid vectors particularly phagemid vectors pBluescript® K/S and pGEM®-3Zf (i.e. only ori from filamentous bacteriophage; please refer to column 76; lines 55-67; column 77, lines 1-4; column 106) wherein the construct comprising gIII-binding domain would be inserted into the multiple cloning site for phage display (i.e. plasmid would then contain only ori and gIII of filamentous bacteriophage; please refer to columns 53-59, section IV.B). Further, Ladner et al. specifically state that while certain phagemids are not preferred for their purposes (i.e. controlling mutations via random mutagenesis of a limited number of

predetermined codons; please refer to column 1, lines 40-52) because coinfections could lead to genetic recombination (i.e. non-controlled mutation), phagemids are suitable for developing a gene that causes a binding domain to appear on the surface of phage-like genetic packages (please refer to the paragraph spanning columns 76 and 77). Thus, if controlled mutagenesis is not contemplated (i.e. presently claimed method), a phagemid vector would be suitable for phage display of binding domains.

Contrary to applicant's assertion, the section IV.B of the Ladner reference does not only discuss M13 phage in general. The Ladner reference teaches gIII of M13 is an excellent choice of outer surface protein to cause protein display (e.g. Col.54, lines 49+). In addition, the Ladner reference also teaches the Bluescript K/S is the preferred phagemid vector (e.g. col.76, lines 60+). The Ladner reference also teaches various suitable cloning vectors (such as the Bluescript K/S) are used for inserting the listed "osp" (outer surface protein) (e.g. col.76, lines 15+). As discussed in col. 54, lines 49+, the M13 gIII coat protein is a preferred "osp", the Ladner reference inherently teach a phagemid vector (based on Bluescript K/S) comprising the M13 gIII.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Parmley, Ladner (WO) and Geider

7. Claims 45, 46 and 48-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parmley et al (Gene. Vol. 73: 305-318; 1988; cited in IDS entered 2/1/2000), in view of Ladner et al (WO 88/06630; 9/7/1988; cited in IDS entered 2/1/2000) and Geider et al (Gene. Vol.33: 341-349; 1985), and if necessary in view of Mead et al (Biotechnology. Vol.10: 85-102; 1988).

Parmley et al, throughout the publication, teach phage displaying antigens, which are screened for specific binding antibodies (Abstract).

The reference teaches inserting a nucleic acid encoding for an antigen (such as fragments of β-gal protein) (e.g. p. 307, col. 1, para 1), which the antigen reads on the "one member of a specific binding pair" of **clm 54** because the antigen binds to a specific antibody (i.e. the other member of the "specific binding pair").

The reference teaches using filamentous phage and fusing the antigen with the Gene III coat protein (e.g. p. 310), which reads on the phage and the gene III coat protein of **clm 54**.

The reference also teaches using host cells to grow the phage particles (e.g. p. 306, col. 2), which reads on the "recombinant host cells" of **clm 54**.

The reference also teaches using the genome of phage (e.g. p. 306; pp. 310-311), which reads on the phagemid genome of **clm 54**.

The reference also teaches mutating the insertions (e.g. p.307), which reads on the limitation of **clm 45**.

Pamley et al., do not explicitly teach using phage particles to display antibody (or immunoglobulin "binding domains", as recited in **clms 46**, **48** and **49**, and more specifically,

scFv molecules as recited in **clms 50-53**. The reference also does not explicitly teach using phagemid as recited in **clm 54**.

However, Ladner et al, throughout the publication, teach using phage (lamda phage) to display antibody fragments such as single chain antibodies (e.g. Abstract, pp.2-3). The reference teaches generating a large repertoire of genes encoding for single chain antibodies and displaying the antibodies on the surface of the phage (e.g. p. 4; Figure 3).

Geider et al, teach using plasmids containing the origin of replication from phage as the only DNA sequence from phage as cloning vector (e.g. Abstract). The reference teaches vectors or plasmids containing the origin of replication from bacteriophage fd such as the vector pfdA1 (e.g. p.341, right col; pp.342-343 bridging). The reference also teaches the generated vectors such as pfdA1 can be used for "insertion of foreign DNA" (pp.342-343; Figure 2). The reference also teaches using helper phage to facilitate the expressing and packaging of the viral progeny (e.g. p.343). The reference also teaches the pfd vectors offer a convenient tool for subcloning of restriction fragments (e.g. p.348).

Mead et al, provide a review of various phage vectors including various phagemid that comprise only the origin of replication (e.g. pp.92+). The reference also teaches using helper phage for the phagemid cloning method (e.g. p.98). The reference also teaches various advantages of using phage vectors including providing a convenient source for single stranded cloned DNA (e.g. p.87+).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to generate recombinant cells comprising phagemid (plasmid

vector comprising phage origin of replication) to clone "binding domains" of antibodies or immunoglobulins, or single chain antibodies as fusion proteins with the phage gIII coat protein.

A person of ordinary skill in the art would have been motivated at the time of the invention to use filamentous phage display method to generate recombinant cells comprising antibody binding domains or single chain antibodies, because phage display allow efficient screening of large library of proteins, as taught Parmley et al (p. 316), and phage displaying antibodies would have the advantages such as creating a diverse population of antibodies, as taught by Ladner et al (e.g. p. 4). It would have been obvious to a person of ordinary skill in the art to try to use one type of phage (filamentous phage) to display antibodies that were already shown to be successfully displayed by another type of phage (lambda phage), as a person with ordinary skill has good reason to pursue the known options within his or her technical grasp.

A person of ordinary skill in the art would have been motivated at the time of the invention to use filamentous phage display method using phagemid as the cloning vector for inserting the DNA of interest such as the gene encoding for fusion proteins between phage gIII coat protein and antibody fragments, because Geider et al and Mead et al teach using a phagemid vector (i.e. a plasmid comprising the phage origin of replication) to clone DNA of interest is routine and known and offers the advantages of being a convenient and safe cloning vectors, as discussed supra. Because all of the references Parmley, Ladner, Geider and Mead teach methods of using phage vectors to clone and express DNA of interest, especially both Parmley and Geider use filamentous phage vectors, it would have been obvious to one skilled in the art to substitute one phage vector (phage vector with complete or substantial amount of phage genome) for the

other (using phage vector containing the minimum required origin of replication) to achieve the predicable result of displaying or expressing the protein (or fusion protein) of interest.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications, because Parmley et al have shown that different proteins with different sequences and/or sizes can be successfully displayed in phage, Ladner et al have shown that antibodies can be successfully displayed in phage, and Geider (or Mead) has shown that cloning and expressing DNA as discussed above.

Discussion and Answer to Argument

8. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants traversed the above rejection by arguing each reference alone. (Reply, pp.7+).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants argue the Parmley reference teaches "denatured peptide", which does not read on the specific binding domain. (Reply, p.7).

Applicants have not provided any evidence to indicate that the displayed proteins/peptides of the Parmley reference are "denatured". The partial β-gal protein of the Parmley reference is displayed as part of the fusion protein (with gIII coat protein), which necessitate the β-gal protein (or fragments thereof) to be displayed as a separate protein domain. In order for the fusion proteins to be successfully displayed on the phage, the fusion proteins must be properly expressed and folded into 3-D structures.

Thus, the fusion proteins of the Parmley are properly folded regardless what portion of the β-gal proteins are expressed. According to the definition of a "domain" (provided by applicants; see Reply filed on 10/17/07, p.6), a domain can be "part" of a polypeptide chain and does not have to be the full protein. As long as the protein fragments are properly displayed into a three dimensional structure, the protein fragments are considered as domains.

The term "domain" is defined in a bochemistry textbook as "A distinct structural unit of a polypeptide; domains may have separate functions and may fold as independent, compact units" (Lehninger et al., Principles of Biochemistry. 2nd ed., 1993, title page, copy right page and p.G-4 only; cited previously). Thus, as long as the reference teaches a unit of a polypeptide that is structurally distinct, the reference teaches a "domain" according to the customary and ordinary meaning of the term. Giving the broadest reasonable interpretation of the instant claims in light of the instant specification, the term "domain" can be broadly interpreted to be any fragment of a polypeptide that forms a distinct structural unit.

"During patent examination, the pending claims must be given the broadest reasonable interpretation consistent with the specification. In re Morris, 127 F.3d 1048, 1054, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997); In re Prater, 415 F.2d 1393, 162 USPQ 541 (CCPA 1969)."

Applicants also assert "no folding" of the protein would have been required for the protein's binding to its antibodies. However, applicants have not provided any supporting evidence to indicate the said assertion.

Applicants pointed to page 9 of the previous Office action for the citation of Smith (Reply, p.8).

It is noted that the citation of Smith in the previous Office action was a typographic error. See the above discussion for the corrected citation.

Applicants also assert Ladner does not teach phage displaying antibodies (Reply, pp.9+).

As discussed above and previously, the Ladner reference teaches displaying antibody on the outer surface of phage. Applicant's statement of "There is no enabling disclosure in Ladner WO of the display of any antibody molecules on the surface of any microorganism" is in direct contradiction to the explicit teachings of the Ladner reference. The Ladner reference explicitly teaches "This invention comprises a genetically engineered organism displaying the expression product of an inserted gene on its outer surface. In a preferred embodiment, a single chain antibody is displayed on the outer surface of the genetically engineered microorganism" (Ladner, Abstract; pp.2+). The Ladner reference further teaches the "microorganism" is a bacteriophage (e.g. p.7).

Although the Ladner reference does not explicitly teach using filamentous phage to display antibodies, the teachings of the Ladner provide motivation to using phage, in general, to display antibodies on the outer surface of microorganism, (in particular, on phage outer

surfaces). A person of ordinary skill in the art would have been motivated at the time of the invention to use filamentous phage display method to generate recombinant cells comprising antibody binding domains or single chain antibodies, because phage display allow efficient screening of large library of proteins, as taught Parmley et al (p. 316), and phage displaying antibodies would have the advantages such as creating a diverse population of antibodies, as taught by Ladner et al (e.g. p. 4). It would have been obvious to a person of ordinary skill in the art to try to use one type of phage (filamentous phage) to display antibodies that were already shown to be successfully displayed by another type of phage (lambda phage), as a person with ordinary skill has good reason to pursue the known options within his or her technical grasp.

Applicants traversed over the Geider and Mead reference by arguing the said references do not teach "display functional specific binding domains". (Reply, pp.11+).

Again, applicants are traversing the above rejection by arguing each reference alone. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants are respectfully directed to the above discussion regarding protein "domains".

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible

harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5,871,907

10. Claims 54, 46, 47 and 49-53 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of U.S. Patent No. 5,871,907. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '907 patent read on or is obvious over the instant claimed invention.

The '907 patent claims using host cells comprising vectors containing genes encoding for binding pairs and gIII coating proteins expressed as fusion proteins (e.g. claims 1, 4, and 13), which the vectors read on the nucleic acids of the instant claim 54.

The '907 patent claims using filamentous phage vectors including phagemid vectors (e.g. claims 11-13), which reads on the filamentous phage of the instant claim 54.

The '907 patent claims the vector (or the phagemid) contains "an origin of replication" of for phage (e.g. claim 4), which read on the origin of replication of the instant claim 54.

The '907 patent also claims the binding pairs are antibody fragments or single chain antibodies (e.g. claims 9 and 25), which read on the instant claims 46, 47 and 49-53.

5,858,657

11. Claims 45-54 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 9-12 and 23-25 of U.S. Patent No. 5,858,657 in view of Geider et al (Gene. Vol.33: 341-349; 1985), and if necessary in view of Mead et al (Biotechnology. Vol.10: 85-102; 1988).

The '657 patent claims method of producing specific binding pair using phage particles or phagemid vector as the expression vectors, and using host cells (or recombinant cells) comprising the said vectors (e.g. Claims 1 and 3), which the used vectors read on the nucleic acid and the recombinant cells of the instant claims.

The '657 patent also claims the vectors comprising genes encoding for fusion polypeptides between the antibodies (or specific binding pair) and the geneIII capsid protein of phage (e.g. claim 12), which read on the nucleic acids of the instant claims.

The '657 patent also claims the phage vectors are selected from filamentous phage (e.g. claim 10), which reads on the filamentous phagemid of the instant claims.

The '657 patent claims using phagemid vector and helper phage (e.g. claim 3), which reads on the phagemid and helper phage of the instant claims.

The '657 patent does not explicitly claims using a phagemid vector comprising the phage origin of replication as the only phage DNA in the vector.

However, Geider et al, teach using plasmids containing the origin of replication from phage as the only DNA sequence from phage as cloning vector (e.g. Abstract). The reference teaches vectors or plasmids containing the origin of replication from bacteriophage fd such as the vector pfdA1 (e.g. p.341, right col; pp.342-343 bridging). The reference also teaches the generated vectors such as pfdA1 can be used for "insertion of foreign DNA" (pp.342-343; Figure 2). The reference also teaches using helper phage to facilitate the expressing and packaging of the viral progeny (e.g. p.343). The reference also teaches the pfd vectors offer a convenient tool for subcloning of restriction fragments (e.g. p.348).

Mead et al, provide a review of various phage vectors including various phagemid that comprise only the origin of replication (e.g. pp.92+). The reference also teaches using helper phage for the phagemid cloning method (e.g. p.98). The reference also teaches various advantages of using phage vectors including providing a convenient source for single stranded cloned DNA (e.g. p.87+).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use phagemid vector comprising the origin of replication from phage.

A person of ordinary skill in the art would have been motivated at the time of the invention to use filamentous phage display method using phagemid as the cloning vector for inserting the DNA of interest such as the gene encoding for fusion proteins between phage gIII coat protein and antibody fragments, because Geider et al and Mead et al teach using a phagemid vector (i.e. a plasmid comprising the phage origin of replication) to clone DNA of interest is routine and known and offers the advantages of being a convenient and safe cloning vectors, as

discussed supra. Because all of the references, the '657 patent, Geider and Mead teach methods of using phage vectors to clone and express DNA of interest, especially both the '675 patent and Geider use filamentous phage vectors, it would have been obvious to one skilled in the art to substitute one phage vector (phage vector with complete or substantial amount of phage genome) for the other (using phage vector containing the minimum required origin of replication) to achieve the predicable result of displaying or expressing the protein (or fusion protein) of interest. A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications.

Other Related Patents

12. Claims 45-54 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of U.S. Patent Nos. 6,916,605; 7,063,943; 6,544,731; 6,521,404; 6,291,650; 6,225,447 and 5,837,242 in view of Geider et al (Gene. Vol.33: 341-349; 1985), and if necessary in view of Mead et al (Biotechnology. Vol.10: 85-102; 1988).

The listed patents contain claims substantially similar to the claims of the '657 or the '907 patent (discussed above). All of the listed patents contain claims either drawn to methods of generating phage displayed fusion proteins, or to products of phage displayed fusion proteins using host cells or recombinant cells. The said reference patents also claim antibodies, fragments thereof, or single chain antibodies are part of the fusion proteins that are encoded by the nucleic acids comprised within the phage vectors.

Although the said patents do not explicitly claim using phagemid vectors comprising the origin of replication from phage as the only phage nucleic acids, it would have been prima facie obvious to use such as phage vector in view of Geider et al, as discussed supra.

5,885,793

13. Claims 45-54 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-41 of U.S. Patent No. 5,885,793 in view of Geider et al (Gene. Vol.33: 341-349; 1985), and if necessary in view of Mead et al (Biotechnology. Vol.10: 85-102; 1988).

The '793 patent claims method of producing specific binding pair using phage particles or phagemid vector as the expression vectors, and using host cells (or recombinant cells) comprising the said vectors (e.g. Claims 1 and 2), which the used vectors read on the nucleic acid and the recombinant cells of the instant claims.

The '793 patent also claims the vectors comprising genes encoding for fusion polypeptides between the antibodies (or specific binding pair) and a component of phage such as geneIII capsid protein (e.g. claim 2 and preferred embodiment in spec., col.22), which read on the nucleic acids of the instant claims.

The '793 patent also claims the phage vectors are selected from filamentous phage (e.g. claims 1 and 2), which reads on the filamentous phagemid of the instant claims.

The '793 patent claims using phagemid vector and helper phage (e.g. claims 1 and 2; preferred embodiment in spec., col.22+), which reads on the phagemid and helper phage of the instant claims.

The '793 patent does not explicitly claims using a phagemid vector comprising the phage origin of replication as the only phage DNA in the vector.

However, Geider et al, teach using plasmids containing the origin of replication from phage as the only DNA sequence from phage as cloning vector (e.g. Abstract). The reference teaches vectors or plasmids containing the origin of replication from bacteriophage fd such as the vector pfdA1 (e.g. p.341, right col; pp.342-343 bridging). The reference also teaches the generated vectors such as pfdA1 can be used for "insertion of foreign DNA" (pp.342-343; Figure 2). The reference also teaches using helper phage to facilitate the expressing and packaging of the viral progeny (e.g. p.343). The reference also teaches the pfd vectors offer a convenient tool for subcloning of restriction fragments (e.g. p.348).

Mead et al, provide a review of various phage vectors including various phagemid that comprise only the origin of replication (e.g. pp.92+). The reference also teaches using helper phage for the phagemid cloning method (e.g. p.98). The reference also teaches various advantages of using phage vectors including providing a convenient source for single stranded cloned DNA (e.g. p.87+).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use phagemid vector comprising the origin of replication from phage.

A person of ordinary skill in the art would have been motivated at the time of the invention to use filamentous phage display method using phagemid as the cloning vector for inserting the DNA of interest such as the gene encoding for fusion proteins between phage gIII coat protein and antibody fragments, because Geider et al and Mead et al teach using a phagemid

vector (i.e. a plasmid comprising the phage origin of replication) to clone DNA of interest is routine and known and offers the advantages of being a convenient and safe cloning vectors, as discussed supra. Because all of the references, the '657 patent, Geider and Mead teach methods of using phage vectors to clone and express DNA of interest, especially both the '675 patent and Geider use filamentous phage vectors, it would have been obvious to one skilled in the art to substitute one phage vector (phage vector with complete or substantial amount of phage genome) for the other (using phage vector containing the minimum required origin of replication) to achieve the predicable result of displaying or expressing the protein (or fusion protein) of interest. A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications.

Discussion and Answer to Argument

14. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants requested the ODP rejections be held in abeyance. Applicants have not provided any specific traversal over the above ODP rejection. Thus, the above ODP rejections are maintained for the reasons of record.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SUE LIU/
Primary Examiner, Art Unit 1639
3/26/09